UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/943,531	08/30/2001	Carl Risinger	SGL-2020-UT	9953

47328 7590 06/29/2006

BIOTECHNOLOGY LAW GROUP
C/O PORTFOLIOIP
PO BOX 52050
MINNEAPOLIS, MN 55402

EXAMINER	
BAUSCH, SARAE L	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 06/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/943,531	RISINGER ET AL.	
	Examiner	Art Unit	
	Sarae Bausch	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-10,13 and 14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-10, 13-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The examiner reviewing your application at the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to examiner Sarae Bausch.

1. This action is in response to papers filed on 04/10/2006. Currently claims 7-10 and newly added claims 13-14 are pending. Claims 1-6 and 11-12 have been cancelled.

2. All the amendments and arguments have been thoroughly reviewed but were found insufficient to place the instantly examined claims in condition for allowance. The following rejections are either newly presented, as necessitated by amendment, or are reiterated from the previous office action. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is Final.**

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 7-10 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for determining a Caucasian human's capacity to metabolize omeprazole, a substrate of the CYP2C19 enzyme, by identifying the two polymorphic sites in the 5' flanking region of CYP2C19 at positions 352 and 1060 of SEQ ID NO:1, but does **not** reasonably provide enablement for;

- Detecting the above capacity to metabolize any substrate of CYP2C19, besides omeprazole.
- Detecting more than the two or more polymorphic sites of 352 and 1060 of SEQ ID No. 1 in any CYP2C19 5' flanking region.
- Determining any capacity(UEM/EM/PM/IM) to metabolize a substrate with any nucleotide present(or haplotype represented) by positions 352 and 1060.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. **It is noted that this rejection was previously presented in section 2, pages 2-9 of the previous office action mailed 12/09/2005 and has been rewritten to accommodate the amendment to claim 7 and newly added claims 13 and 14.**

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and breadth of claims

Claims 7-10 and 13-14 are broadly drawn to a method of determining a Caucasian's capacity to metabolize any substrate of CYP2C19 through the identification of any two or more polymorphic sites in any 5' flanking region of CYP2C19. The claims are so broad as to encompass the method's execution with; any haplotype located in a "CYP2C19 5' flanking region" and detecting the above capacity to metabolize any substrate of CYP2C19. However, as will be further discussed, there is no support in the specification and prior art for the methods as broadly as they are currently claimed. The invention is in a class of invention that the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The unpredictability of the art and the state of the prior art

The specification recites that "for these experiments, a single dose of 20 mg omeprazole(Losec, AstraZeneca) was given in the morning after an overnight fast"(lines 10-12 pg. 13), and furthermore that "in the first part of the study, approximately 90 samples(Swedish Caucasians) were selected as set forth in Table 1"(Spec pg. 13). In table 11, the specification teaches the statistically relevant p-values of haplotypes H1-H3 as defined in Table 10 also on page 19 of the specification. However, the specification does not teach that any haplotype or any polymorphism located at positions 352 and 1060 correlate with every capacity to metabolize omeprazole. In table 13 on page 20, the specification teaches the CYP2C19 genotypes and haplotypes that are associated with a particular capacity to metabolize omeprazole, the only taught substrate of CYP2C19, (i.e. Ultra Extensive Metabolizers(UEM), Extensive metabolizers(EM), Intermediate metabolizers(IM), or Poor metabolizers(PM) along with the observed metabolic ratios of omeprazole. The specification teaches only particular nucleotides, and particular haplotypes to be correlated with a particular ability to metabolize. However, there

is no teaching of any other SNP in the flanking region of CYP2C19, besides those enumerated in Table 10, that are associated with an observed capacity to metabolize omeprazole. Furthermore, only a single population of Swedish Caucasians is taught to be a part of the specification's findings. Lastly, only omeprazole is taught as a substrate of CYP2C19 to yield these metabolic capacities. The specification omits any teachings of results obtained with a diverse population of all races, testing for metabolic capacities achieved by treatment with a diverse group of substrates of CYP2C19 other than omeprazole, and any SNP located in the flanking region of CYP2C19.

First, regarding the unpredictability associated with claiming any SNP located in the flanking region of CYP2C19, there exists a large body of knowledge in the prior art related to polymorphisms in general, and their association with diseases or disease states. The art is highly unpredictable with regard to the functionality of polymorphic sites in genomic DNA. After a screening assay identifies polymorphisms, it is unpredictable whether any such polymorphisms would be associated with any phenotypic trait, such as a disease state or a physiological state. For example, Hacker et al. were unable to confirm an association between a gene polymorphism and ulcerative colitis in a case where prior studies suggested such a relationship would exist since the relationship had been identified in a different population (Gut, 1997, Vol. 40, pages 623-627). Even in cases where an association between a particular gene and a disease state is known to exist, such as with the LPL gene and heart disease risk or the p-globin gene and sickle cell anemia, researchers have found that when using SNP (single nucleotide polymorphism analysis) it was difficult to associate SNPs with disease states or to even identify key genes as being associated with disease (Pennisi, Science, 281 (5384):1787-1789). Finally, in some cases where multiple polymorphisms are identified in a gene, some of these are demonstrated to be disease associated and some are not. Blumenfeld et al. (WO 99/52942) disclose a number of polymorphisms in the FLAP gene. While Blumenfeld et al. were able to demonstrate that some

of these polymorphisms are associated with patients having asthma but some of these are not (see Figure 3). For example, the marker 10-35/390 was demonstrated to be associated with asthma, with a p value of 0.00229, while the marker 10-33/327 was determined to not have a statistical association with asthma (p=0.294). Thus, even for SNPs within the same gene, it is highly unpredictable as to whether a particular marker will be disease associated. As a result, there is a great deal of unpredictability that exists in the invention without any guidance in the specification for example, to any polymorphism located in the flanking region of CYP2C19 gene other than those enumerated in Table 10 of the specification, being correlated to any metabolic capacity. With respect to the unpredictability involved with the claims recitations of this method being applicable to a human of any race, additional prior art corroborates the unpredictability in Goldstein et al's teaching that "the frequency of this polymorphism[that of CYP2C19] varies markedly in different racial populations, with the PM phenotype representing 2-5% in Caucasian populations, but from 13-23% in Oriental populations"(Pharmacogenetics, 1997, 7; page 59 bottom right). Goldstein et al. further teach that "the present results indicate complete concordance between phenotype and genotype in three Oriental racial groups, while the incidence of the CYP2C19m1 allele is higher in Oriental races than in Caucasians or African-Americans...Saudi Arabians were found to resemble Caucasians in both the incidence of CYP2C19m1 and relative absence of CYP2C19m2"(Goldstein et al, Pg 63 bottom left side). Concerning the substrate being claimed, applicant provides no teaching of a general quality had by every substrate that their claim presently reads on. As a result, the presently filed specification provides enablement for only that of omeprazole.

The post filing date art further supports the unpredictability involved in extrapolating the results of a study with one distinct Caucasian population to all races as Ozawa et al. teach "that it is a matter of primer importance to take interracial differences into account in the frequency of genetic polymorphisms of drug-responsive genes"(Introduction, Drug Metab. Pharmacokin.

19(2); 83-95(2004). The reference continues by teaching that ethnic differences in "Chinese, African, Swedish, and Spanish are schematically outlined in Fig. 1...that clearly indicated the existence of a considerable number of poor metabolizers showing high metabolic ratios in European Caucasians(Swedish and Spanish) at a frequency of approximately 7% but PMs are relatively rare in the Chinese(1%)"(Page 84 left side).

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there are a significant number of parameters which would have to be studied to apply this method to the broadly claimed embodiments involving any SNP in the 5' flanking region of CYP2C19, in any race, and with any substrate to CYP2C19. The quantity of experimentation required to discover how to use the instant invention is very high. In order to use the claimed invention as asserted by the specification, one would have to establish a relationship between non-existent SNPs in the 5' region flanking CYP2C19 with some capacity to metabolize omeprazole, or some other substrate of CYP2C19. In order to obtain the type of information necessary to practice the claimed invention, one would be required to undertake the screening of hundreds or thousands of patients of all races as well as possible hundreds of pharmaceutical agents. Even if such experiments were undertaken, it would still be unpredictable as to whether any associations would still be detected considering the new diversity of experimental variables, and further in light of the unpredictability of such associations, as already discussed. Thus, while one could perform further research to determine whether applicant's method is useful as broadly as it is claimed, it is unknown as to what the outcome of such research might be and as to whether any quantity of experimentation would result in the identification of an association between the polymorphism in any race and to any capacity for metabolism. This would require years of

inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Working Examples

The specification has no working examples of the method using any SNP in the region flanking the CYP2C19 gene, using any population other than a Swedish Caucasian one, to detect a capacity for metabolizing any substrate other than omeprazole.

Guidance in the Specification.

The specification provides no evidence that the disclosed method would be effective if practiced as broadly as it is claimed. The guidance provided by the specification amounts to an invitation for the skilled artisan to try and follow the disclosed instructions to make and use the claimed invention. The specification merely discloses that "for these experiments, a single dose of 20 mg omeprazole(Losec, AstraZeneca) was given in the morning after an overnight fast"(lines 10-12 pg. 13), and furthermore that "in the first part of the study, approximately 90 samples(Swedish Caucasians) were selected as set forth in Table 1"(Spec pg. 13). In table 11, the specification teaches the statistically relevant p-values of haplotypes H1-H3 as defined in Table 10 also on page 19 of the specification. In table 13 on page 20, the specification teaches the CYP2C19 genotypes and haplotypes that are associated with a particular capacity to metabolize omeprazole, the only taught substrate of CYP2C19, (i.e. Ultra Extensive Metabolizers(UEM), Extensive metabolizers(EM), Intermediate metabolizers(IM), or Poor metabolizers(PM) along with the observed metabolic ratios of omeprazole. Even if, arguendo, the detected SNPs in the flanking region of CYP2C19 are correlated with some capacity of metabolism, there is no support for the same, prophetic correlation in any race being studied.

Most importantly, there exists much unpredictability within the specification's teachings. For example the claims are generally drawn to all polymorphisms at the two positions, 352 and 1060. No specific nucleotide/haplotype is recited to be correlated with a particular marker of capacity. In addition, Table 13 also teaches that the markers are dependent on not only which single haplotype is present, but which pair of haplotypes are present. For example, an H2 being present could represent "UEM/EM", "UEM and EM", or "EM and (IM)", depending on the copy number. It is highly unpredictable to claim solely the present of any polymorphism, since each one(in specific haplotypes and present in specific copy numbers) correlates with particular markers.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, in a highly unpredictable art where the use of SNPs to detect disease states is even further unpredictable, the factor of unpredictability weighs heavily in favor of undue experimentation. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Response to Arguments

The response traverses the rejection on page 4-8 of the response mailed 04/10/2006. The response asserts that the results of the working example of the claimed method are enabled. The response points to the results in table 13 on page 20 of the specification and asserts that the specification provides specific guidance with population studies, haplotype analysis, and methodology. This response has been thoroughly reviewed but not found persuasive. The specification does not provide specific guidance with detecting the capacity to metabolize any substrate of CYP2C19 by detecting any haplotype of any two or polymorphic sites. The specification does not teach a study that predictably correlates a haplotype of CYP2C19 to determine a Caucasian's capacity to metabolize CYP2C19. The specification teaches in example 3 the haplotype analysis on 232 individuals and identifying 5 haplotypes, however one of the haplotypes was excluded due to low frequency and the other haplotype (H4) was not included in the predictive haplotypes studied (see table 12). The specification only sets forths statistical p-vales between CYP2C19 haplotypes and omeprazole (see table 11). Therefore, not every haplotype with a polymorphism as position 352 and 1060 has the ability to predictably correlate a Caucasian's capacity to metabolize any substrate of CYP2C19.

The response asserts on page 5-6 that Omeprazole is representative of other substrates. The response asserts that omeprazole is a model drug that represents CYP2C19 metabolic properties of many other drugs and assert that it is a marker drug and useful "probe". This response points to Andersson et al, Baleine et al, Evans et al. to support this assertion. This response has been thoroughly reviewed but not found persuasive. Andersson et al. teach administration of only omeprazole and in this study found that Chinese metabolized omeprazole

slower than Caucasians (see page 29, 1st column, 1st full paragraph), which does not substantiate the assertion that other drugs represent CYP2C19 metabolism. Baleine et al. teach that 3 out of 62 white population were poor metabolizes of omeprazole (5%) and a total of 8 out of 77 total individuals studied were poor metabolizes (10%) while 3 out of 122 white population were poor metabolizes of mephenytoin (2.5%) and a total of 7 out of 142 total individuals were poor metabolizes (5%), which suggests that less than half of the total population that are poor metabolizes of omeprazole are poor metabolizes of mephenytoin (see table 1, page 664). If CYP2C19 would metabolize a substrate with the same capacity, it would be expected that 10% of the total study assayed would be poor metabolizes of mephenytoin as well, which was not presented in Baleine et al, Baleine et al. teach in table 1 that only 5% of the total study assayed were poor metabolizes of mephnytoin which does not suggest that mephenytoin and omeprazole are metabolized in the same capacity and do not appear to act predictably. Further, Baleine et al. teach that further population studies are necessary to determine the sensitivity and specificity of CYP2C19 genotyping procedures for predicting the poor metabolizes phenotype (see page 668, 1st column, 3rd full paragraph). Evans et al. compares Mephenytoin and dextromethorphan and appears to obtain different results. Furthermore, Evans does not compare omeprazole to either of these two drugs. The response asserts that Chang et al. report better separates from poor metabolizes using omeprazole as a more advantageous probe. However, the claims are drawn to the capacity of a Caucasian to metabolize any substrate of a CYP2C19 enzyme and Chang does not teach a representative number of drugs that are metabolized by CYP2C19 in order to determine a Caucasians capacity to metabolize any substrate of a CYP2C19 enzyme. Therefore,

the art teaches the unpredictability of whether different drugs have differing effects on metabolism.

The response asserts that the haplotypes of two or more positions are enabled. Applicant request clarification of the office alleging any two or more polymorphic sites in a CYP2C19 flanking region is not enabled by the specification as the claims recite predicting the metabolic capacity based upon a haplotype containing two or more polymorphic sites wherein the sites are specified and assert that the two positions specified enable the predictive methods of claim 7. The response asserts that any other polymorphic sites added to the haplotype would be expected to boost the predictive value. This response has been thoroughly reviewed but not found persuasive. First, the claims do not recite specific nucleotide/haplotypes and read on additionally polymorphisms located within the 5' flanking region of SEQ ID No. 1. The examiner asserted that no specific nucleotide/haplotype is recited to be correlated with a particular marker of capacity (see rejection above). In addition, Table 13 teach that the markers are dependent on not only which single haplotype is present, but which pair of haplotypes are present. For example, an H2 being present could represent "UEM/EM", "UEM and EM", or "EM and (IM)", depending on the copy number. It is highly unpredictable to claim solely the present of any polymorphism, since each one(in specific haplotypes and present in specific copy numbers) correlates with particular markers. Secondly, additional polymorphic sites located within the 5' flanking region of CYP2C19 may not necessarily increase the predictive value of determining the capacity to metabolize a substrate. Single point mutations can have deleterious effects and may not enhance the predictive value. Furthermore, even if the region specified in Figure 1 of the 5' flanking region of CYP2C19 is not so large that additional polymorphisms could be

identified and requires routine experimentation, it would require trial and error and is it not predictable to determine or identify which additional polymorphisms will increase, decrease, or have no effect on the capacity to metabolize any substrate of CYP2C19. It is not clear which polymorphism would create a haplotype and what the capacity to metabolize a substrate would be. Furthermore, the specification teaches that two out of the 5 haplotypes that were assayed for the ability to determine the capacity to metabolize a substrate were not predictive (see table 11 and 13 and page 18-19) and therefore support the assertion that additional polymorphisms, even within the specified haplotypes assayed, are not predictably correlative to determining a capacity to metabolize any substrate of a CYP2C19 enzyme.

The response asserts on page 7 that determining the metabolic capacity is enabled. The response asserts that the office alleged that determining any capacity to metabolize a substrate with any nucleotide or haplotype represented at positions 352 and 1060 is not enabled by the specification and applicant request clarification. The specification is only enabled for the specific substrate, omeprazole and the examiner asserts that the specification does not enable one to determine any capacity to metabolize a substrate with any nucleotide or haplotype represented at positions 352 and 1060 because the specification only teaches statistically significant data with determining the capacity of omeprazole with H1, H2 and H3 (see table 11).

The response asserts that example 3 and table 13 show that metabolic ratio can be predicted effectively when a haplotype from each chromosome is determined and assert that several haplotype combinations encompassed by the pending claims are provided in the specification and other haplotype combinations can be utilized for the claimed methods and the specification provides guidance for their selection. This response has been thoroughly reviewed

but not found persuasive. The specification teaches two out of the five haplotypes were not predictive of metabolic capacity (see table 11) where H4 haplotype is not predictably correlative to metabolic capacity of omeprazole and therefore is not predictably effective in determining the capacity to metabolize a substrate of CYP2C19. Even within the claimed haplotype, it is not predictive to determine a Caucasian's capacity to metabolize any substrate of a CYP2C19 enzyme by identifying any haplotype of two or more polymorphic sites comprising 352 and 1060 of SEQ ID No. 1.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Conclusion

5. No claims are allowable.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarae Bausch whose telephone number is (571) 272-2912. The examiner can normally be reached on M-F 10am-7pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER

Sarae Bausch, PhD.
Examiner
Art Unit 1634